

PATENT COOPERATION TREATY

MAY 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)Applicant's or agent's file reference
see form PCT/ISA/220Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)FOR FURTHER ACTION
See paragraph 2 belowInternational application No.
PCT/JP2005/001444International filing date (day/month/year)
26.01.2005Priority date (day/month/year)
29.01.2004International Patent Classification (IPC) or both national classification and IPC
A61K31/4468, A61P9/00Applicant
OTSUKA PHARMACEUTICAL CO., LTD.

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
 Box No. II Priority
 Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 Box No. IV Lack of unity of invention
 Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 Box No. VI Certain documents cited
 Box No. VII Certain defects in the international application
 Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Pacreu Largo, M
Telephone No. +49 89 2399-7851



WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/001444

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - in written format
 - in computer readable form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2005/001444

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims 1-4
 No: Claims

Inventive step (IS) Yes: Claims 1-4
 No: Claims

Industrial applicability (IA) Yes: Claims 1-4
 No: Claims

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Reference is made to the following documents:
D1 : PATENT ABSTRACTS OF JAPAN, vol. 1995, no. 03, 28 April 1995 (1995-04-28) & JP 06 340627 A (OTSUKA PHARMACEUT CO LTD), 1994-12-13
D2 : SUN BING ET AL: "OPC-28326, a selective femoral vasodilator, is an alpha2C adrenoceptor-selective antagonist" FASEB JOURNAL, vol. 15, no. 5, 8 March 2001 (2001-03-08), page A915, XP002325918 & Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biol; Orlando, Florida, USA; MARCH 31-APRIL 04, 2001
D3 : WARE J A ET AL: "ANGIOGENESIS IN ISCHEMIC HEART DISEASE" NATURE MEDICINE, NATURE PUBLISHING, CO, US, vol. 3, no. 2, February 1997 (1997-02), pages 158-164, XP002074058
2. Document D1 discloses the use of compounds of present formula (I) as peripheral vasodilating agents.

Document D2 refers to the compound of present claim 2, also known as OPC-28326 as a vasodilator, selective for the femoral artery, and therefore, as a good candidate to treat peripheral arterial occlusive diseases or other vasospasms disorders.

None of the documents of the search report disclose or suggest the use of compounds of formula (I) for promoting angiogenesis.

Thus, the subject-matter of claims 1-4 appears to be novel and to involve an inventive step, Art. 33(2) and (3) PCT.

Re Item VI

Certain documents cited

- IMAIZUMI TAKASHI ET AL: "OPC-28326, a selective peripheral vasodilator, possesses an angiogenic property." JOURNAL OF PHARMACOLOGICAL SCIENCES, vol. 94, no. Supplement 1, 2004, page 155P, XP009046812 & 77TH ANNUAL MEETING OF THE JAPANESE PHARMACOLOGICAL SOCIETY; OSAKA, JAPAN; MARCH 08-10, 2004 ISSN: 1347-8613
- HASHIMOTO AYAKO ET AL: "OPC-28326, a selective peripheral vasodilator, possesses a stabilizing effect on newly formed microvessels." JOURNAL OF PHARMACOLOGICAL SCIENCES, vol. 94, no. Supplement 1, 2004, page 156P, XP009046811 & 77TH ANNUAL MEETING OF THE JAPANESE PHARMACOLOGICAL SOCIETY; OSAKA, JAPAN; MARCH 08-10, 2004 ISSN: 1347-8613

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/001444

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2005/001444

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	1-4
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-4
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-4
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)
and / or
2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Reference is made to the following documents:
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Document D2 refers to the compound of present claim 2, also known as OPC-28326 as a vasodilator, selective for the femoral artery, and therefore, as a good candidate to treat peripheral arterial occlusive diseases or other vasospasms disorders.

None of the documents of the search report disclose or suggest the use of compounds of formula (I) for promoting angiogenesis.

Thus, the subject-matter of claims 1-4 appears to be novel and to involve an inventive step, Art. 33(2) and (3) PCT.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

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Re Item VI

Certain documents cited

- IMAIZUMI TAKASHI ET AL: "OPC-28326, a selective peripheral vasodilator, possesses an angiogenic property." JOURNAL OF PHARMACOLOGICAL SCIENCES, vol. 94, no. Supplement 1, 2004, page 155P, XP009046812 & 77TH ANNUAL MEETING OF THE JAPANESE PHARMACOLOGICAL SOCIETY; OSAKA, JAPAN; MARCH 08-10, 2004 ISSN: 1347-8613
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